

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 11, 12, 14, 15, 17-22, 59, 63-67, and 76-79 are pending in the application, with claims 11, 12, 18 and 20 being the independent claims. Claims 10, 13, 47 and 80-85 have been canceled. Claims 11, 12, 14, 17, 18, 20, 63-67, 76, 78 and 79 have been amended. Support for the claim amendments may be found in the original claims and throughout the specification. Thus, no new matter is added by way of these amendments, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider and withdraw the outstanding rejections.

I. *Claim Rejection Under 35 U.S.C. § 102(e)*

Claims 10-15, 17-20, 47, 59, 66, 67, 80 and 83 were rejected under 35 U.S.C. § 102(e) as being anticipated by Horn et al. (U.S. Patent No. 6,465,175) (Office Action, pages 3-4). Claims 10, 13, 47, 80 and 83 have been canceled herein, thus rendering the rejection moot as it pertains to these claims. Applicants respectfully traverse the rejection as it applies to the remaining claims.

Claims 11 and 12 recite methods that result in “synthesized nucleic acid molecules comprising said one or more oligonucleotides.” The “one or more oligonucleotides” refers to “fluorescently labeled oligonucleotides.” Thus, the claimed methods incorporate a

fluorescently labeled oligonucleotide into a synthesized nucleic acid. In contrast, the methods referred to by Horn result in the synthesis of nucleic acids that do not include a fluorescently labeled oligonucleotide. The fluorescently labeled probes used in the Horn methods are not extendible and are not incorporated into the synthesized nucleic acid molecules. Horn makes this clear in Example 5 at column 17, stating “the 3’ end of the probe is blocked from extension by the 3’ phosphate.” Thus, the Horn methods do not anticipate claims 11 and 12 or any claim dependent thereon.

Claim 18 recites a method that results in the extension of detectably labeled primers to form nucleic acids that are detectably labeled. For the reasons discussed in the preceding paragraph, the Horn methods do not anticipate claim 18 or any claim dependent thereon.

Claim 20 recites a method for detecting an *increase* in fluorescence associated with the hybridization of a fluorescently labeled oligonucleotide to a target nucleic acid. In contrast, Horn refers to fluorescently labeled oligonucleotides that undergo a *decrease* in fluorescence upon hybridization to a target nucleic acid. Horn makes this clear, for example, in the Abstract at column 3, lines 7-20, and in claim 1. Thus, the Horn methods do not anticipate claim 20 or any claim dependent thereon.

Applicants therefore request reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(e).

II. Claim Rejections Under 35 U.S.C. § 103(a)

Claims 63-65 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Horn *et al.* Office Action, pages 5-7. Applicants respectfully traverse this rejection. As discussed above, Horn *et al.* does not teach or suggest all of the elements of claims 11, 12, 18 or 20. Therefore, Horn *et al.* necessarily does not teach all of the elements of claims 63-65 which depend from claims 11, 12, 18 or 20. A *prima facie* case of obviousness requires that all of the limitations of the claims be taught or suggested by the cited references. Since Horn *et al.* does not teach or suggest all of the elements of claims 63-65, a *prima facie* case of obviousness has not been established. Applicants therefore request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

III. Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claims 10-15, 17-22, 47, 59, 63-67 and 76-80 were rejected under 35 U.S.C. § 112, first paragraph. Claims 10, 13, 47 and 80 have been canceled, thus rendering the rejection moot as it pertains to these claims. Applicants respectfully traverse the rejection as it applies to the remaining claims.

Applicant's specification fully enables the claimed methods for detectably labeled oligonucleotides, including fluorescently labeled oligonucleotides. Nonetheless, in an effort to expedite prosecution of the application, Applicants have amended the claims to recite the use of fluorescent labeled oligonucleotides.

The use of oligonucleotides labeled with any fluorescent label is clearly enabled by Applicant's specification. The specification discloses a large number of fluorescent labels in

Table 1, pages 63-65, and exemplifies the use of fluorescein in Examples 4, 7, 9-11, TAMRA in Example 5, BODIPY in Example 6, and FITC in Example 8. Claims 11, 12 and 18 recite a detectable change in fluorescence; a change that may be either an increase or decrease in fluorescence. While it is true, as noted in the Office Action, that the location of a fluorescent label in an oligonucleotide can affect the nature of the observed change in fluorescence upon hybridization of the oligonucleotide to a target nucleic acid, Applicant's specification states at page 65, lines 5-7 that "one of ordinary skill in the art can easily determine using art-known techniques of spectrophotometry, which of the above identified fluorophores or combinations thereof can be used in accordance with the invention." In addition, the examples provided in the Applicant's specification provide specific guidance as to what changes in fluorescence upon hybridization may be expected when oligonucleotides are labeled at different positions.

Thus, guided by Applicant's specification, the skilled artisan can identify fluorescent labels that result in a detectable change in fluorescence upon hybridization of a labeled oligonucleotide to a target nucleic acid without undue experimentation, and can also identify the optimal location of the fluorophore (e.g., 5' end, 3' end, or internal) for obtaining the desired change in fluorescence without undue experimentation.

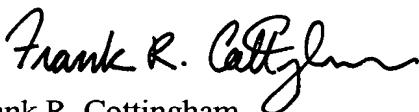
Applicants therefore request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider and withdraw all presently outstanding rejections. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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